

**AMENDMENT**

**U.S. Appln. No. 09/423,093**

**REMARKS**

In paragraph 2, on page 2 of the Office Action, the Examiner maintains the rejection of Claims 85-106 under 35 U.S.C. § 112, first paragraph as failing to comply with the written description requirement.

Specifically, it is the Examiner's position, as set forth at page 9 of the Office Action, that the specification does not provide written description support for the expression "at least about 10 nucleotides in length", i.e., it is the Examiner's position that the specification only provides support for about 10 to about 20 nucleotides in length (page 10, lines 9-11).

For the following reasons, Applicants respectfully traverse the Examiner's rejection.

The test for sufficiency of support in an application is whether the disclosure of the application relied upon "reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter" (*In re Kaslow*, 217 USPQ 1089 (Fed. Cir. 1983)).

As stated by the Federal Circuit in *Ralston Purina Company v. Far-Mar-Co., Inc.*, 227 USPQ 177 (Fed. Cir. 1985):

Far-Mar-Co cites several range cases to support its argument that ranges found in the applicant's claim language must correspond exactly to ranges disclosed in the parent. These cases are not on point. The facts in these cases precluded a determination that one skilled in the art could derive the claim limitations from the parent, due to a number of different factors, e.g., the unpredictable nature of the art, *In re Sichert*, 566 F.2d 1154, 196 USPQ 209 (CCPA 1977); failure to distinguish one process from another, *In re MacLean*, 454 F.2d 756, 172 USPQ 494 (CCPA 1972); the addition of a critical limitation, *In re Blaser*, 556 F.2d 534, 194 USPQ 122 (CCPA 1977); failure to define a critical term, *In re Lukach*, 442 F.2d 967, 169 USPQ 795

**AMENDMENT**

**U.S. Appln. No. 09/423,093**

(CCPA 1971); and use of a list that did not contain the claimed substance. *In re Ahlbrecht*, 435 F.2d 908, 168 USPQ 293 (CCPA 1971). In addition, a predecessor to this court has held "that a claim may be broader than the specific embodiment disclosed in a specification is in itself of no moment." *In re Rasmussen*, 650 F.2d 1212, 1215, 211 USPQ 323, 326 (CCPA 1981)...

[T]he court did not clearly err in determining that the parent's disclosure adequately supported the water ranges of "at least about 25% by weight," and "at least 25% by weight." [where the examples of the parent application showed a water content that equaled 25% and 27%]. (Emphasis added)

There is no unpredictable nature with respect to the size of the oligonucleotide of the present invention, as it is well-known in the art that probes can be greater than 20 nucleotides. Further, the upper limit of the size of the probe is not relevant to distinguishing over the prior art, i.e., such is not a critical limitation or a critical term.

The specification, at page 5, teaches that the nucleic acids may be variable in length, and that in one embodiment, they are from about 10 to about 20 nucleotides in length. Thus, the range of "about 10 to about 20" is merely an example of one embodiment. Further, the examples in the present application teach that the oligonucleotides can be 10 or greater nucleotides in length, and can be greater than 20 nucleotides (e.g., positions 11821-11844 of SEQ ID NO:1 (i.e., 24 amino acids) and positions 12945-12924 of SEQ ID NO:1 (i.e., 22 amino acids)).

Similarly, in *In re Wertheim*, 191 USPQ 90 (CCPA 1976) the asserted claims covered a range ("solids level of at least 35%"), whereas the specification disclosed a range ("concentrated . . . until a concentration of 25 to 60% solid matter is reached").. The court held that the claim found written description in the specification even though the claims was not repeated verbatim in the specification.

**AMENDMENT**

**U.S. Appln. No. 09/423,093**

On page 11 of the Office Action, the Examiner notes Applicants' argument that Claim 88 provides support for the breadth of the claims. However, the Examiner contends that Claim 88 is not an original claim, but was added to the application on June 21, 2002, and thus can not be relied upon for support.

However, as Applicants previously argued, the examples and Claim 88 provide support for a oligonucleotide of larger than 20 nucleotide bases. The Examiner has not rejected Claim 88 as containing new matter, i.e., such is supported by the examples in the specification. Thus, the present application clearly provides support for oligonucleotides of more than 20 nucleotide bases.

More specifically, positions 11821-11844 of SEQ ID NO:1 (i.e., 24 amino acids) and positions 12945-12924 of SEQ ID NO:1 (i.e., 22 amino acids) are taught in Table 5, 12<sup>th</sup> row, 3<sup>rd</sup> column of the specification.

Nonetheless, in order to advance prosecution, Applicants hereby amend the claims to set forth a range of about 10 to 28 nucleotides, support which can be found in Tables 5 and 5A of the present specification, rows *wbdL* and *wbdM* where the forward primers are 18 and 23 nucleotides in length and the reverse primers are 28 and 21 nucleotides in length, respectively. Again, the specific size of oligonucleotide is not critical to the present invention.

In view of the amendments to the claims, Applicants respectfully submit that this aspect of the Examiner's rejection has been rendered moot.

**AMENDMENT**

**U.S. Appln. No. 09/423,093**

In addition, the Examiner maintains the rejection with respect to Claim 101 and the expression "sugar-pathway genes". Specifically, the Examiner contends that the specification does not provide an adequate written description of the essential starting materials where the bacterial strain is well-known at the time of filing nor provide an adequate written description for those materials which have yet to be discovered.

In view of the amendment to Claim 101 to recite that the sugar-pathway gene specific to the bacterial strain to be detected is selected from the group consisting of *rmlB*, *rmlD*, *rmlA*, *rmlC*, *glf*, *manC*, *manB*, *ddhD*, *ddhA*, *ddhB*, *ddhC* and *abe* (support for which can be found in the Table at pages 52-58 of the present specification), Applicants respectfully submit that this aspect of the Examiner's rejection has been rendered moot.

Accordingly, Applicants respectfully submit that the claims have adequate written description, and thus request withdrawal of the Examiner's rejection.

In paragraph 15 of page 13 of the Office Action, the Examiner rejects Claims 85-106 under 35 U.S.C. § 103 as being unpatentable over Fratamico et al in view of Liu et al and Brennan.

Specifically, the Examiner states that Fratamico et al discloses a method whereby nucleic acids from various bacterial strains are amplified via PCR and are subsequently detected (see Table 1 and column 5, which teach detecting nucleic acids derived from *E. coli* serotype 0111). The Examiner notes that Fratamico et al does not identify "sugar-pathway genes", such as *wzx*. However, the Examiner contends that Lui et al teaches

**AMENDMENT**

**U.S. Appln. No. 09/423,093**

sugar-pathway genes of bacteria that exhibit O-antigens are of significant interest and that O-antigen gene clusters of several *E. coli* serovar, including O111 have been sequenced, and studied and Lui et al explicitly teaches the gene *wzx* as having been studied.

Furthermore, the Examiner states that Brennan discloses an array of nucleic acids which comprises all possible oligonucleotides of 10 nucleotides in length, and discloses every gene identified in the claims, including those sequences that hybridize under the specified conditions.

Hence, the Examiner concludes that it would have been obvious to have modified the teachings of Fratamico et al such that samples could be tested for the presence of *E. coli* expressing the bacterial polysaccharide O-antigen serotype O111 as Lui et al teaches that such nucleic acids have been isolated and characterized, and the probes and primers for doing such existed in the prior art as taught by Brennan.

For the following reason, Applicants respectfully traverse the Examiner's rejection.

Fratamico et al discloses certain oligonucleotide primers, which can be used to detect *E. coli* using polymerase chain reaction. The primers were selected from portions of the DNA fragments of the plasmid of *E. coli*, and are not the same primers as recited in the claimed invention. The plasmid in Fratamico et al is specific to only one pathogenic form of *E. coli* (EHEC).

In contrast, the present invention relates to the improved specificity of the detection and identification of O-antigens

**AMENDMENT**

**U.S. Appln. No. 09/423,093**

(see page 7, lines 5-10 of the present specification). Applicants have indicated that these O-antigens may be used in stereotyping, i.e., identifying an antigenic property, of all *E. coli*. Thus, the method of the presently claimed invention is specific for the O-antigen, and the claims have been amended to clearly set forth such.

Applicants respectfully submit that Table 1 on column 3 and column 5, lines 39-40, of Fratamico et al does not teach the skilled person the advantages of the present invention, nor does it suggest modifying the invention disclosed therein to provide the presently claimed invention.

Accordingly Applicants respectfully submit that the present invention is not taught or suggested in the Fratamico et al, and for the following reasons, it is clear that Liu et al and Brennan do not provide the deficiencies that exist therein.

Lui et al teaches the *wzx* gene, and that this gene encodes for a flippase for O-unit translocation. However, Lui et al does not teach or suggest oligonucleotides, much less sequence data of the gene. Furthermore, the fact the *wzx* gene encodes a protein that is a flippase has little relevance in predicting whether this gene would be useful in determining O-antigen specificity.

Thus, while Lui et al discloses the *wzx* gene, it does not teach or suggest to one skilled person that this gene may be a suitable target for identifying *E. coli*, especially as the oligonucleotides employed in the presently claimed invention are not disclosed in Lui et al.

**AMENDMENT**

**U.S. Appln. No. 09/423,093**

As to Brennan, this reference discloses a method for conducting a large number of chemical reactions on a support surface and particularly a method of producing an array plate. The abstract indicates the method also extends to sequencing oligonucleotides and identifying amino acid sequences that bind to biologically active macromolecules. Column 3, lines 10-35, indicates how this method may be employed.

The Examiner states on page 14, paragraph 20, of the Office Action that Brennan discloses "every 10-mer probe and primer encompassed by the Applicants' method". However, this is an erroneous analysis because while Brennan discloses methods of identifying amino acid sequences that bind to a biologically active macromolecule it does not disclose the sequences of the probes and primers themselves. Rather, Brennan simply invites the skilled person to set up a research program to identify suitable primers and oligonucleotides that bind to biologically active molecules.

Brennan does not teach or suggest the presently claimed invention, even if combined with Fratamico et al, as neither teaches the claimed oligonucleotides which are specific for the O-antigens.

Furthermore, the Examiner has not provided sufficient motivation for one skilled in the art to combine Fratamico et al, Lui et al and Brennan to achieve the present invention. The skilled person does not work out of curiosity, and given that Fratamico et al does not identify the disadvantages of the method therein, such as the lack of specificity of the primers disclosed therein, a skilled person

**AMENDMENT**

**U.S. Appln. No. 09/423,093**

has no reason to look for alternatives to the method of identifying *E. coli* disclosed by Fratamico et al.

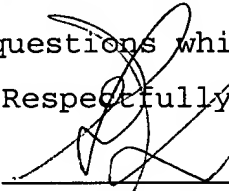
The Examiner should be reminded that when considering whether the presently claimed invention is obvious, it is impermissible to use hindsight.

Accordingly Applicants respectfully submit that the present invention is not taught or suggested in Fratamico et al, alone or when combined with the teachings of Liu et al and Brennan, and thus request withdrawal of the Examiner's rejection.

In view of the amendments to the claims and the arguments set forth above, reexamination, reconsideration and allowance are respectfully requested.

The Examiner is invited to contact the undersigned at his Washington telephone number on any questions which might arise.

Respectfully submitted,

  
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